

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)	
)	
Jong-Soo Woo et al.)	Group Art Unit: 1612
Serial No.: 10/599,500)	
)	Examiner: GiGi Huang
Filed: September 29, 2006)	

For: CONTROLLED RELEASE FORMULATION FOR ORAL
ADMINISTRATION OF METFORMIN

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. §1.132

Sir:

I, Jong-Soo Woo, being a citizen of the Republic of Korea and presently residing at Daewol Maeul 821-105, #914, Jeongja-dong, Jangan-gu, Suwon-si, Kyungki-do, 440-330, Republic of Korea, do declare:

That I am one of the co-inventors of the invention disclosed in the above-identified application, and hence am fully familiar with the subject matter therein; and

That I have conducted an experiment as follows, in order to demonstrate the remarkable effect of the inventive composition having the specific weight ratio of a polyethylene oxide ("PEO"):a natural gum (i.e., 0.27:1 to 1.6:1).

<Preparation of comparative compositions>

A tablet having each of the compositions listed in Table 1 was prepared by repeating the procedure of Example 1.

Table 1

Ingredients		Content(wt%)			
		Comparative (i)	Comparative (ii)	Comparative (iii)	Comparative (iv)
Granule forming part	Metformin-HCl	50	50	50	50
	Polyethylene oxide (Polyox [®] WSR, M.W. 5,000,000)	2.5	1.4	9.6	10
Mixture part	Polyvinylacetate/ Polyvinyl pyrrolidone mixture	20	20	20	20
	Wax	13	13	13	13
	Xanthan gum	12.5	13.6	5.4	5
	Silicon dioxide	1	1	1	1
	Magnesium stearate	1	1	1	1
Total		100	100	100	100
PEO:natural gum		0.2:1	0.1:1	1.8:1	2.0:1

<In vitro release-tests for the tablets prepared in Comparative Examples (i) to (iv) and Example 1>

In vitro release-tests were conducted for the tablets prepared in Comparative Examples (i) to (iv) above and Example 1 described in the specification by repeating the method of Test Example 1 described in the specification.

As can be seen from Figs 1 and 2 below, both of the formulations of Comparative Examples (i) and (ii) having weight ratios below 0.27:1 and those of Comparative Examples (iii) and (iv) having weight ratios above 1.6:1 exhibit an initial burst

release of metformin, which may cause gastrointestinal adverse effects, as compared in the inventive formulation of Example 1.

Fig 1

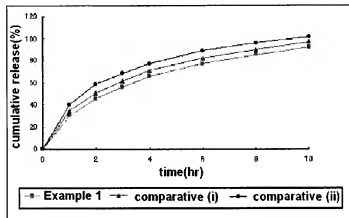
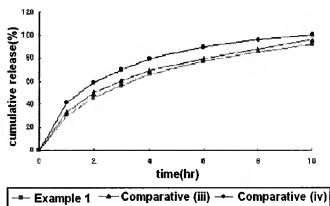


Fig 2



The remarkable effect obtained in the range of 0.27:1 to 1.6:1 as a PEO:a natural gum can be more clearly recognized in view of the comparison of $t_{90\%}$ (time to 90% drug release) between the formulations of Examples 1 to 12, and those of Comparative Examples 1, 2 and (i) to (iv).

Table 2

	Weight ratio (PEO:natural gum)	t ₉₀ %
Example 1	0.8:1	>10
Example 2	0.5:1	10
Example 3	0.5:1	10
Example 4	0.5:1	9
Example 5	1:1	>10
Example 6	1:1	10
Example 7	0.8:1	>10
Example 8	0.8:1	>10
Example 9	1.6:1	10
Example 10	0.44:1	10
Example 11	0.63:1	>10
Example 12	0.27:1	>10
Comparative Example 1	0:1	6
Comparative Example 2	1:0	5
Comparative Example (i)	0.2:1	8
Comparative Example (ii)	0.1:1	6
Comparative Example (iii)	1.8:1	8
Comparative Example (iv)	2.0:1	6

* Examples 1 to 12 and Comparative Examples 1 and 2 are described in the specification.

As can be seen from Table 2 above, the inventive formulations having the weight ratio of 0.27:1 to 1.6:1 show desired t₉₀% values ranging from approximately 9 to 10 hours, while the t₉₀% values of the comparative formulations are not more than 8 hours.

Therefore, it is clear that the selection of the range of 0.27:1 to 1.6:1 as the weight ratio of a PEO:a natural gum leads to a remarkable increase in the controlled release effect of the formulation.

I hereby declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and, further,

that these statements made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of Unites States Code and that such willful false statements may jeopardize the validity of the application or any patents issuing thereon.

Further the deponent saith not.

Date: 10th day of June, 2008

J. S. Woo

(Jong-Soo Woo)